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PCT/KR2004/002888

PATENT COOPERATION TREATY

PCT

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference PCA31170-NCC	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. **PCT/KR2004/002888**	International filing date *(day/month/year)* **09 NOVEMBER 2004 (09.11.2004)**	Priority date *(day/month/year)* 11 NOVEMBER 2003 (11.11.2003)

International Patent Classification (IPC) or national classification and IPC

C07K 14/47(2006.01)i

Applicant

NATIONAL CANCER CENTER et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
12 SEPTEMBER 2005 (12.09.2005)	28 FEBRUARY 2006 (28.02.2006)
Name and mailing address of the IPEA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer PARK, JEONG UNG Telephone No. 82-42-481-8159

Form PCT/IPEA/409 (cover sheet) (April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/KR2004/002888

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4)
- ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this reort as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☐ the description:
pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the claims:
pages _____ as originally filed/furnished
pages* _____ as amended (together with any statment) under Article 19
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the drawings:
pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets _____
- ☐ the sequence listing *(specify)* : _____
- ☐ any table(s) related to sequence listing *(specify)* : _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to sequence listing *(specify)* : _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 9,10

because:

☒ the said international application, or the said claims Nos. 9,10 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

Claims 9,10 relate to a method of treatment of the human or animal body and according to Art.34(4)(a)(i) and Rule 67.1(iv) PCT, the IPEA is not required to carry out an international preliminary examination on this claims.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☐ no international search report has been established for said claims Nos. _____

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Istructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Istructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b) and 13ter.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the techmical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/KR2004/002888

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8	YES
	Claims		NO
Inventive step (IS)	Claims	1-8	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-8	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The present invention relates to a neutralizing chimeric antibody against hepatocyte growth factor (HGF) for preventing and treating intractable diseases and cancers that are caused by binding of HGF to its receptor Met.

The following documents have been considered for the purpose of this report:

D1: Cao, B., et al., PNAS, 98(13): 7443-7448 (Jun 2001)
D2: Tokunou, M., et al., Am J Patbol., 158(4): 1451-1463 (Apr 2001)
D3: Popkov, M., et al., J Mol Biol., 325: 325-335 (Jan 2003)

1. Novelty

D1 describes the neutralizing monoclonal antibodies (mAb) to hepatocyte growth factor/scatter factor (HGF/SF) display antitumor activity in animal models. D1 also show that no single mAb was capable of neutralizing the in vitro activity of HGF/SF, and that the ligand possesses a minimum of three epitopes that must be blocked to prevent Met tyrosine kinase activation. D2 relates to inhibition effect by addition of neutralizing mAb against HGF in myofibroblasts. The use of neutralizing chimeric mAb against a epitope of HFG having the amino acid sequence of SEQ ID No: 32 or 33 as a single agent is not disclosed in any of the prior art. Therefore, the subject-matter of claims 1-8 is considered to be novel under PCT Article 33(2).

2. Inventive Step

D3 discloses that three or more of the epitopes, possibly two for the Met receptor and one for heparin, need to be blocked in order to inhibit HGF activity in vivo and in vitro, and a mixture of at least 3 mAbs is capable of neutralizing HGF in an in vitro experiment. However, D3 provides a monoclonal antibody that can neutralize HGF as a single agent and inhibit cell scattering activity in vitro. Therefore, the subject-matter of claims 1-8 is considered to involve an inventive step under PCT Article 33(3).

3. Industrial Applicability

The subject-matter of claims 1-8 is considered to be industrially applicable under PCT Article 33(4).